

PC-0040 CIP

**REMARKS**

Applicants have canceled claims 13-20 without prejudice to renewal and reserve the right to pursue these claims in subsequent divisional applications. Applicants have amended claims 2 and 7 to clarify the invention. Applicants have submitted new claims 21-23. Support for new claim 21 is found in the specification on page 2, lines 22-23. Support for new claims 22 and 23 is found on page 9, lines 22-23.

Applicants have amended the specification to correct sentence duplication and inadvertent errors. Support for the amendment of paragraph 2 on page 9 is found in EXAMPLE VIII, on page 33, lines 27-28. No new matter has been entered by these amendments to the specification and claims.

For the Examiner's convenience, Applicants have attached an automated alignment (phrap) to show the approximate location of each of the claimed fragments, SEQ ID NO:3-8, with respect to SEQ ID NO:2, the nucleic acid molecule of claim 2. Please note, this is not an exact alignment and was not done with the same software that was used to hand-edit the full length sequence filed in the original application in 1997.

**CONCLUSION**

In light of the above amendments and remarks, Applicants submit that the present application is in condition for allowance. Early notice to that effect is earnestly solicited. If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Agent of Record. Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. 09-0108.

Respectfully submitted,  
INCYTE GENOMICS, INC.

Date: *22 July 2002*

*Lynn E. Murry*

Lynn E. Murry, PhD  
Reg. No. 42,918  
Direct Dial Telephone: (650) 845-4159

3160 Porter Drive  
Palo Alto, California 94304  
Phone: (650) 855-0555  
Fax: (650) 844-4166

PC-0040 CIP

**"VERSION WITH MARKINGS TO SHOW CHANGES MADE"****IN THE SPECIFICATION**

Please amend the second paragraph on page 9, beginning on line 11 as shown below:

The transcripts which encode the cancer [protein] protein were expressed in cDNA libraries associated with secretion, immune response, and cancer. The expression pattern closely resembles that for other tumor antigens which are expressed in cancers and is at least two-fold higher than that of other tissues in the category. Example VIII shows in detail how differential expression separates the indicated cancer from other cancers or disorders that may occur in or be associated with a particular tissue. For example, the percent abundance of the cDNA in transitional cell cancer of the bladder is more than two-fold higher than expression in the bladder tissue of the subject with cystitis or cytologically normal tissue from a subject with bladder [prostate] cancer. Furthermore, the transcript was never expressed in seven other normal tissues (not shown). The tissue description for the three libraries shown in the northern analysis is quite specific and supports the use of the cDNA, the protein and antibody which specifically binds the protein as diagnostics for transitional cell carcinoma of the bladder. Specific expression data is shown for each of the other cancers--lymphoma, metastatic adenocarcinoma of the colon, Wilm's tumor, renal cell carcinomas, metastatic endometrial cancer, and testis tumor-- in which the cDNA, the protein and antibody are useful as cancer diagnostics. It must also be noted that the transcript encoding the cancer marker protein was not distinctly expressed in other cancers of the brain, breast, prostate, small intestine, stomach, and uterus or in normal or diseased bone, heart, muscle, or neurons.

Please amend the second paragraph on page 17, line 13, as shown below.

Detection and quantification of a protein using either labeled amino acids or specific polyclonal or monoclonal antibodies are known in the art. Examples of such techniques include two-dimensional polyacrylamide gel electrophoresis, enzyme-linked immunosorbent assays (ELISAs), radioimmunoassays (RIAs), and fluorescence activated cell sorting (FACS). These assays and their quantitation against purified, labeled standards are well known in the art. (Ausubel, supra, unit 10.1-10.6). ~~A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering epitopes is preferred, but a competitive binding assay may be employed. (See, e.g., Coligan et al. (1997) Current Protocols in Immunology, Wiley-Interscience, New York NY, and Pound, supra).~~

PC-0040 CIP

## IN THE CLAIMS

Please amend claims 2 and 7 as shown below:

2. (Once Amended) An isolated cDNA comprising a nucleic acid sequence selected from:
  - a) SEQ ID NO:2 and the complement of SEQ ID NO:2 [thereof]; and
  - b) a fragment of SEQ ID NO:2 selected from SEQ ID NOs:3-8 and the complements of SEQ ID NOs:3-8 [thereof; and
  - c) a variant of SEQ ID NO:2 selected from SEQ ID NOs:9-11 and the complements thereof].
7. (Once Amended) A method for using a cDNA to detect expression of a nucleic acid in a sample comprising:
  - a) hybridizing the composition of claim 3 to nucleic acids of the sample under conditions to form hybridization complexes; and
  - b) detecting hybridization complex formation, wherein complex formation indicates expression of a nucleic acid complementary to the cDNA of the composition in the sample.

Assembly: Aligned reads (Bold = start for cDNA relative to the full length CB1)

1573677CB1

1573677X13

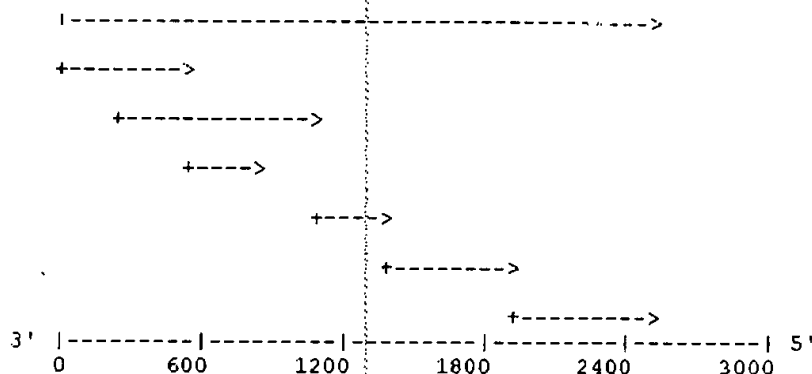
065573R1

1854560F6

228382R6

040360R1

1456688F1



1573677X13 caaaaggacaagataataaagtacaaaatggttcgttacatcagaaggatacagttcatgacaatgactt  
1573677CB1 caaaaggacaagataataaagtacaaaatggttcgttacatcagaaggatacagttcatgacaatgactt  
10 20 30 40 50 60 70

1573677X13 tgagccctacettactggacagtcacaatcagagtaacagttacccctcaatgagcgacccctacctgtcc  
1573677CB1 tgagccctacettactggacagtcacaatcagagtaacagttacccctcaatgagcgacccctacctgtcc  
80 90 100 110 120 130 140

1573677X13 agctattacccgcgcgtccattggatttccctactccctcaatgagggtccgtggtctactgcaggggacc  
1573677CB1 agctattacccgcgcgtccattggatttccctactccctcaatgagggtccgtggtctactgcaggggacc  
150 160 170 180 190 200 210

1573677X13 ctccgattccatacctcaccacctaaggacagctcagtaacggagaccatcattttatgcacgatgctgt  
1573677CB1 ctccgattccatacctcaccacctaaggacagctcagtaacggagaccatcattttatgcacgatgctgt  
220 230 240 250 260 270 280

1573677X13 ttttgggcagcctgggggcctggggaacacatctatcagcacaggttcaatttttccctgaaaaccct  
1573677CB1 ttttgggcagcctgggggcctggggaacacatctatcagcacaggttcaatttttccctgaaaaccct  
065573R1 .....atttttccctgaaaaccct  
290 300 310 320 330 340 350

1573677X13 gcgtttctcagcatgggggacaagtgggtctcaaggctcagcagaccagagctccgcgtatgggagcagct  
1573677CB1 gcgtttctcagcatgggggacaagtgggtctcaaggctcagcagaccagagctccgcgtatgggagcagct  
065573R1 gcgtttctcagcatgggggacaagtgggtctcaaggctcagcagaccagagctccgcgtatgggagcagct  
360 370 380 390 400 410 420

1573677X13 acacctacccccagagctccctgggtggcaggttggtgatgggcagccagggctttcacagcgacaccc  
1573677CB1 cccccagcttttggtcaaccgcagtatcagagccctcagcagccacccagacccgctgggttgccccac  
065573R1 cccccagcttttggtcaaccgcagtatcagagccctcagcagccacccagacccgctgggttgccccac  
430 440 450 460 470 480 490

1573677X13 tcagcaaggncccccgggatgaacagcctggagcagggcatggttgacctgaagattggggacgtcagct  
1573677CB1 gcaacagaaacgcggcggtttgggcagagcggaggggctggcagcgatagcaactctcctggaaacgtcca  
065573R1 gcaacagaaacgcggcggtttgggcagagcggaggggctggcagcgatagcaactctcctggaaacgtcca  
500 510 520 530 540 550 560

1573677X13 gcctcngcngtcaagacgtgggctctgtctcagcagcgtggcactgactggtgtcttttttggcaacggt  
1573677CB1 gcctaatcttgcctccagcgtcgatccaccccgctccttgaaaaactgaaggctgctcacagctacaac  
065573R1 gcctaatcttgcctccagcgtcgatccaccccgctccttgaaaaactgaaggctgctcacagctacaac  
570 580 590 600 610 620 630

1573677X13 ggga.....  
1573677CB1 ccgaaagaggtttgagtggaatctgaaaaagcgggcgtgtgttcacatcacaagagctactctgaggacgaca  
065573R1 ccgaaagaggtttgagtggaatctgaaaaagcgggcgtgtgttcacatcacaagagctactctgaggacgaca  
1854560F6 .....gtttgagtggaatctgaaaaagcgggcgtgtgttcacatcacaagagctactctgaggatgaca  
640 650 660 670 680 690 700

1573677CB1 tccaccgctccatttaagtactccatctggtgttagcacagagcacggcaacaagcgccctgg\*acagcgcc  
065573R1 tccaccgntccatttaagtactccatctggtgttagcacagagcacggcaacaagcgccctgggacacggct  
1854560F6 tccaccgctccatttaagtactccatctggtgttagcacagagcacggcaacaagcgccctgg\*acagcgcc  
710 720 730 740 750 760 770

1573677CB1 tccgctgcatgagcagcaa\*ggggcccgctt\*acctgctcttcag\*cgtaaa\*tggt\*agt\*gggcattt  
065573R1 tncgctgcatgagcagcaaagggggcccgctcttancgtcttttttagngtcaaatggggagcttnggcattt  
1854560F6 tccgctgcatgagcagcaa\*ggggcccgctt\*acctgctcttcag\*cgtaaa\*tggt\*agt\*gggcattt  
780 790 800 810 820 830 840

1573677CB1 ttgtggggtggccgagatgaagtcccccgctggactacggcaccagtgccggggtctggtctcaggacaag  
065573R1 tttttggggttnggcccagatgnaagnttccccngtngggacttaaggggaaaccaattgcccgggg  
1854560F6 ttgtggggtggccgagatgaagtcccccgctggactacggcaccagtgccggggtctggtctcaggacaag  
850 860 870 880 890 900 910

1573677CB1 tggaaggggaagttttagtgcagtggtttttgttaaggatgtacccaataaccagctccggcacatca  
065573R1 gtnccttgggtctttaaagggacnaaaattnggaaggggggaaaggtttttaaagtgcccaantggggatttt  
1854560F6 tggaaggggaagttttagtgcagtggtttttgttaaggatgtacccaataaccagctccggcacatca  
920 930 940 950 960 970 980

1573677CB1 ggctggagaataacgacaacaaaccggtc\*acaaactccccgggacacccaggaggtgcccttagaaaaag  
065573R1 tttgntttaaagggntttntancccaaaa\*taanccaagntttccnggnaaaaataaagnttttngg  
1854560F6 ggctggagaataacgacaacaaaccggtccacaaactccccgggacacccaggaggtgccct.....  
990 1000 1010 1020 1030 1040 1050

1573677CB1 ccaagcaagtgtctgaaaattatcagttccctacaagcacacaacctccatcttcgacgactttgtcacta  
065573R1 ggaatttaaagggnaaaaaaaacccggtttaaanaaanttccccgggggcaaacccagggggggttc  
1060 1070 1080 1090 1100 1110 1120

1573677CB1 cgagaagcgccagaggaggaggaggtggtgcgaaggaacggcagagtcgaaacaaacaatgagggcgaa  
065573R1 ccccttnggaaaaagggccaaaggaaaantnntttaaatttttaaggttcntaaaaagganaaaaaanc  
228382R6 .....gcgaa  
1130 1140 1150 1160 1170 1180 1190

1573677CB1 ccagttttctacat\*gttctaacgttttgattttgaaaacagtttaaaacacgtgtgcttggtcagctcca  
065573R1 nlcnahtttttngm\*gggggtttttntaaattngggggggggcc.....  
228382R6 ccagttttctacatngttctaacgttttgattttgaaaacagtttaaaacacgtgtgcttggtcagctcca  
1200 1210 1220 1230 1240 1250 1260

1573677CB1 gtgtgtcgtcccggtcggggggttgagtgttgcatctttgcctttcttgcgttgatttttgccagatgg  
228382R6 gtgtgtcgtcccggtcggggggttgagtgttgcatctttgcctttcttgcgttgatttttgccagatgg  
1270 1280 1290 1300 1310 1320 1330

1573677CB1 atctgcatttattttgtactttttctatgtattataatcctgtagaagtcactaataaaggagatattttt  
228382R6 atctgcatttattttgtactttttctatgtattataatcctgtagaagtcactaataaaggagatattttt  
1340 1350 1360 1370 1380 1390 1400

1573677CB1 tttgtcagcttatcaatcagactgatctaatgtgaaatgtaagtatccttaaaaaacaaagcatctatttt  
228382R6 tttgtcagcttatcaatcagactgatctaatgtgaaatgtaagtatccttaaaaaacaaagcatctatttt  
1410 1420 1430 1440 1450 1460 1470

1573677CB1 ggcagaaattgtgttcttaaatcagtcatttgatattctgtgagacttcataatttctcatccctttatt  
228382R6 ggcagaaattgtgttcttaaatcagtcatttgatattctgtgagacttcataatttctcatccct\*atl  
040360R1 .....agtcatttgatattctgtgagacttcataatttctcatcccttall  
1480 1490 1500 1510 1520 1530 1540

1573677CB1 gcttttttagcaaacataagaaccatgagtcattttgtcatttagagtattctgataaaatctcttgaa  
228382R6 gcttttttagcaaacataagaaccatgagtcattttgtcatttagagtattctgataaaatctcttgaa  
040360R1 gcttttttagcaaacataagaaccatgagtcattttgtcatttagagtattctgataaaatctcttgaa  
1550 1560 1570 1580 1590 1600 1610

1573677CB1 atactgaaatcaaaaagggttaattgattttttgttcattctgatttgcattttattatctgttatcggtct  
040360R1 atactgaaatcaaaaagggttaattgattttttgttcattctgatttgcattttattatctgttatcggtct  
1620 1630 1640 1650 1660 1670 1680

1573677CB1 aaagtgtcaattttacccatttgattttttctgtagacagataacttttaatttttcaaatgtggcagaca  
040360R1 aaagtgtcaattttacccatttgattttttctgtagacagataacttttaatttttcaaatgtggcagaca  
1690 1700 1710 1720 1730 1740 1750

1573677CB1 ctttttttttttttttgaataatctttccctccagatctgttgccactgaacagccacccgtccctcact  
040360R1 cttttttttttttttt\*gaataatctttccctccagatctgttgccactgaacagccacccgtccctcact  
1760 1770 1780 1790 1800 1810 1820

1573677CB1 gtccctgggtgccgattgggctggatgggtgtggggcatgatgtgtggaggaaactggaagggtgcttttaggt  
040360R1 glccctgggtgccgattgggctggatgggtgtggggcatgatgtgtggaggaaactggaagggtgcttttaggt  
1830 1840 1850 1860 1870 1880 1890

1573677CB1 ctgggttcagggtcgggcattctttgttgggtgcacatctttttaaatcttacacctttcttaagaattc  
040360R1 ctgggttcagggtcgggcatt\*ctttgttgggtgcacatctttttaaatcttacacctttcttaagaattc  
1456688F1 .....agaattc  
1900 1910 1920 1930 1940 1950 1960

1573677CB1 taatgccgtcttaagtttttataccaataatgctgagctttaagtgtaggatc\*tggtagtacagaca\*g  
040360R1 taangccngcttaagtttttaaccataangctgagctttaagggtagggnccctgg\*aggacagacaag  
1456688F1 laalgccglttlaagtttttataccaataatgctgagctttaagtgtaggatc\*tggtagtacagaca\*g  
1970 1980 1990 2000 2010 2020 2030

1573677CB1 tgtgatggatgatg\*ctgct\*gggtgtaaatctcatcgtgtgtgtctaatcttttttccctgttgaaatggg  
040360R1 tg\*gatgggngaaggcngcttgggtgnaaat\*\*caacggggggg\*cnaaatcttttcccn\*\*tggtatggg  
1456688F1 tgtgatggatgatg\*ctgct\*gggtgtaaatctcatcgtgtgtgtctaatcttttttccctgttgaaatggg  
2040 2050 2060 2070 2080 2090 2100

1573677CB1 taaaaacaaaacaaaacttttttagaagatgaatttgctgtcatgttttgtggaatgagggaaccgttga  
040360R1 aaaaacaaaacaaaacttttttagag.....  
1456688F1 taaaaacaaaacaaaacttttttagaagatgaatttgctgtcatgttttglygaalgagggaaccgttga  
2110 2120 2130 2140 2150 2160 2170

1573677CB1 gctcactaccacctggagtttgagttgaagcatgaaaatggtgcccatgctgacgctccagcgcctgga  
1456688F1 gctcactaccacctggagtttgagttgaagcatgaaaatggtgcccatgctgacgctccagcgcctgga  
2180 2190 2200 2210 2220 2230 2240

1573677CB1 tctgcacgtgcccttgtagaggatccttacgctcctagagagcagacgctttctgaaaactacttgctcc  
1456688F1 tctgcacgtgcccttgtagaggatccttacgctcctagagagcagacgctttctgaaaactacttgctcc  
2250 2260 2270 2280 2290 2300 2310

1573677CB1 aaaagacccctctgagtttaacgtttcagctgtatcattagacttgatatttagagcgtgtcacttcctctga  
1456688F1 aaaagacccctctgagtttaacgtttcagctgtatcattagacttgatatttagagcgtgtcacttcctctga  
2320 2330 2340 2350 2360 2370 2380

1573677CB1 a\*ctgttactgctgaatggagtcctggacgac\*attgggttttt\*cctctaggagaataacaagccttaa  
1456688F1 anctgttactgctgaatggagtcctggacgacnattgggtttttcctctaggagaataacaagccttaa  
2390 2400 2410 2420 2430 2440 2450

1573677CB1 taacaataactatttagca.....  
1456688F1 taacaataactatttagcaaaaaanaaangngmagtganannnnngtnganaa.....  
2460 2470 2480 2490 2500 2510 2520